Reviewing Psychedelic Research: A Guide for IRBs

As research involving psychedelic administration expands, this resource is designed to help IRBs identify key considerations and engage productively with researchers, supporting ethical psychedelic research.

BACKGROUND: PSYCHEDELICS AND PSYCHEDELIC RESEARCH

What Are Psychedelics?

Psychedelics are a class of naturally occurring and synthetic substances that temporarily and profoundly alter or intensify sensory perception (including visual, auditory, or somatic phenomena), self-perception, cognition, and emotion. Commonly studied examples include psilocybin/psilocin, lysergic acid diethylamide (LSD), ayahuasca, dimethyltryptamine (DMT), 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), mescaline, and ibogaine. Psychedelics act on serotonin 2A receptors and interact with a range of neurotransmitter systems. 3,4-methylenedioxymethamphetamine (MDMA), which is known for producing feelings of emotional closeness and empathy, is pharmacologically distinct but is commonly grouped with psychedelics in research and policy contexts.

Risks and Benefits in Research Settings

Most psychedelics studied in research settings are not addictive and carry low toxicity at typical doses, though profiles vary (for example, MDMA has some addictive potential and ibogaine carries cardiac risks requiring careful screening and monitoring). Primary psychedelic risks are psychological, including acute anxiety while under the influence and, in some rare cases, prolonged disturbance, particularly in those predisposed to psychosis. The nature of the psychedelic experience and its risks can be shaped significantly by "set and setting," a phrase used to describe the participant's mindset and expectations and the physical and interpersonal environment of the session. Research suggests that psychedelics may offer benefits for treatment-resistant depression, post-traumatic stress disorder (PTSD), addiction, and end-of-life anxiety, though evidence is still developing. Psychedelics have the potential to produce experiences sometimes described as mystical or spiritually significant, which may result in transformative life changes.

Psychedelic-Assisted Therapy

Psychedelic-assisted therapy (PAT) is one prominent model used in clinical research. PAT is a structured clinical intervention in which a psychedelic is administered in conjunction with psychotherapy or psychological support, including preparatory sessions, monitored dosing sessions, and post-session integration. Research is exploring whether the PAT model is essential for achieving clinical benefit from psychedelics, as well as optimal approaches to therapy.

Legal Status

Psychedelics are currently Schedule I controlled substances in the US. Researchers must hold a DEA Schedule I researcher registration and research institutions must meet DEA storage and handling requirements. Efforts to reschedule some psychedelics are underway, in recognition of potential medical uses, and scheduling will change for any psychedelic drug granted FDA approval. FDA finalized its guidance on psychedelic clinical trials in July 2026, addressing manufacturing standards, clinical pharmacology, blinding challenges, the role of psychotherapy, safety monitoring, and informed consent. Although the use of psychedelics outside a clinical trial remains federally illegal, some US jurisdictions have legalized, decriminalized, or developed regulated access frameworks. State and local provisions do not supersede federal law, including DEA and FDA requirements, but may be relevant to mitigating the legal or social risks of participating in psychedelic research. Several federal and state entities have announced funding for psychedelic research, as well as efforts to facilitate research and prepare for clinical roll out.

Types of Psychedelic Research

In psychedelic administration studies (the focus of this resource), participants receive a psychedelic drug in a controlled research setting; the main considerations are participant risk and consent. In long-term follow-up studies, participants from prior studies or state-licensed programs are followed over time but no drug is administered; primary concerns are data sensitivity and privacy. Social science and observational research may involve surveys or interviews with people who use psychedelics outside research settings or with practitioners; key concerns include participant privacy and self-reported illegal activity.

APPROACHING PSYCHEDELIC RESEARCH WITH APPROPRIATE PERSPECTIVE

Although psychedelic research can raise challenges for IRBs, as described below, it is important to avoid unnecessary exceptionalization.

Consider the following:

- If psychedelic research is unfamiliar, look for analogies to more familiar research. Is psychedelic research truly different? Based on what evidence? Where have you seen similar challenges arise before, and how were they handled?
- Be careful not to assume that psychedelic research is per se more dangerous or more beneficial than other types of clinical or mental health research. Focus on the available evidence and open questions.
- Be mindful of approaches that would exclude vulnerable participants without compelling scientific or ethical reasons. Many psychedelic studies include vulnerable populations, especially those with mental health conditions and terminal diagnoses, with the goal of determining whether and how these interventions may help.

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THE EVOLVING NATURE OF PSYCHEDELIC RESEARCH

The field of psychedelic research is evolving rapidly and some important scientific and ethical questions remain unresolved. Where best practices have not yet been established, the key task for IRBs is to ensure that the researcher's chosen approach is adequately described and justified in relation to participant protection.

Active areas of debate — ask researchers to explain their approach and rationale:

- What is the appropriate approach to consent for the altered states and potential transformative experience induced by psychedelics?
- Is physical touch appropriate during psychedelic administration sessions and how should consent approach this issue?
- What sort of safety monitoring and psychological support should be required for psychedelic administration sessions (how, by whom, for how long, etc.)?
- What counts as a safety concern (adverse event and/or unanticipated problem) when challenging experiences can be expected, participants may not experience effects such as euphoria and hallucinations negatively, and both may be therapeutically important?
- Is therapy an essential adjunct to psychedelic administration? What sort of psychotherapy or psychological support is needed?
- Is it appropriate to include populations unable to consent for themselves, e.g., adolescents or individuals with cognitive impairment?

It is especially important to assess researcher expertise. Have they ever done psychedelic research before? Are they aware of relevant considerations, debates, and essential safeguards? Especially when investigator experience is low and the IRB is unfamiliar with psychedelic research, consider consulting an outside expert to assist with protocol review.

KEY REVIEW CONSIDERATIONS

When reviewing psychedelic research, consider each of the following elements. Examine information provided in the protocol and seek discussions with the research team and/or outside experts.

SCIENCE AND SAFETY PROFILE	
What is known about the effects, risks, and benefits of this psychedelic drug?	Be careful not to over- or under-estimate psychedelic risks. Investigators should provide evidence-based characterizations, including what is known, unknown, and debated. Look for specificity to the drug being studied. Seek clarity regarding what effects are expected, given implications for risk assessment and reporting.
Are proposed risk minimization strategies proportionate to actual risks?	Review screening, contraindications, and drug interactions. Clarify if/when discretion will be permitted to allow enrollment/continued participation following acceptable physical exam. Also examine: • How appropriate "set and setting" (defined above) will be maintained • The role, number, and credentials of facilitators and monitors (FDA guidance calls for observation by 2 monitors for the duration of the administration session: a lead monitor who is a health care provider with graduate-level training and clinical experience in psychotherapy licensed to practice independently and an assistant monitor with a nursing or bachelor's degree and at least 1 year of clinical experience in a licensed mental health care setting) • Approaches to physical touch during administration sessions • Emergency protocols, including possible administration of rescue medicines to block the psychedelic experience and presence of an on-call physician • Discharge criteria following administration • Psychological support • Plans for long-term monitoring, including duration and type (FDA guidance suggests 12 weeks of monitoring for treatment effect, followed by 12 months of long-term follow-up)
What will constitute an unanticipated problem? How will adverse events be defined and addressed?	Challenging psychedelic experiences may be expected and therapeutically important. Ask how the protocol distinguishes these from unanticipated problems that warrant reporting to the IRB and/or intervention. For adverse events, look for a clear, study-specific definition and criteria. (FDA guidance defines AEs to include "any untoward medical occurrence," including euphoria, hallucinations, and cognitive alterations. The guidance further indicates that AEs should be monitored and reported as a safety concern, even if hypothesized to be associated with therapeutic response.)
How does the protocol address blinding?	Participants can often tell whether they are under the influence of a psychedelic drug. Ask how the protocol addresses this, e.g., through use of an active placebo, different dosing levels, or another comparator. If blinding is not possible, ask how the study design otherwise limits bias. (FDA guidance suggests use of blinded central raters, blinding questionnaires, complementary trial designs, etc.) This is important to the IRB's assessment of how the study's potential scientific benefits relate to its risks.
How does the protocol address expectation effects?	Ask what measures will be used to manage expectation effects, i.e., the tendency for participants/investigators to expect benefit from psychedelic intervention. Approaches

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	may include independent outcome assessment, expectancy evaluation surveys, standardized facilitator training, and efforts to minimize therapeutic misconception.
PARTICIPANT VULNERABILITY	
How are participant vulnerabilities identified and addressed?	Consider diagnosis-based vulnerability (e.g., mental health conditions, terminal illness), administration-based vulnerability (e.g., destabilizing effects of the drug while under the influence), and any other special populations enrolled (e.g., adolescents, incarcerated individuals, individuals with cognitive impairment). Avoid reflexive exclusions without compelling justification. Focus on approaches to consent and any special protections that may be important.
INFORMED CONSENT	
How will informed consent be approached given challenges specific to psychedelic research?	Look for at least the following: • How therapeutic misconception and hype will be addressed • Whether consent materials accurately convey scientific uncertainty (e.g., by avoiding/qualifying language about "natural" products or historical use) • How participants will be helped to understand the psychedelic experience before dosing (e.g., changes in perception, cognition, judgment, vulnerability, and suggestibility, as well as ineffability and transformative potential) • How physical touch will be handled during administration sessions • Any constraints imposed on participant decision-making during administration sessions while under the influence of psychedelics (e.g., leaving the facility)
Are consent procedures appropriately tailored for any special populations?	Ask about adjustments for populations with heightened vulnerability. Diagnosis alone (mental health, terminal illness) should not be assumed to impair capacity.
PRIVACY, CONFIDENTIALITY, AND LEGAL/SOCIAL RISKS	
How will privacy and confidentiality be protected?	How will participants reporting illicit drug use be protected? How will session recordings be handled? Have researchers considered whether a Certificate of Confidentiality applies or should be sought?
How will legal, employment, and other social risks to participants be addressed?	Investigators should identify foreseeable risks and describe specific protections or explain why those risks are unlikely given study design and authorization.
If there are deviations from FDA guidance, are they justified?	Investigators should note deviations from FDA's 2026 guidance and explain their rationale. Note that FDA guidance is not legally binding.

ASSISTANCE FROM INSTITUTIONAL OFFICIALS OR COUNSEL

Some elements of psychedelic research may benefit from input beyond the IRB. Consider raising the following with institutional officials or legal counsel, as necessary, without expecting that every psychedelic protocol will need institutional review:

- Local legal status of the study drug(s)
- DEA requirements for researcher licensure and drug storage
- Any special protections that should be offered to participants
- Realistic risks to the institution (reputational, legal) and how to minimize them – while emphasizing that the IRB's responsibility is participant protection

ADDITIONAL RESOURCES

This space is rapidly evolving, making it difficult to suggest enduring resources. However, the following reflect a good place to start:

- FDA Guidance: Psychedelic Drugs — Considerations for Clinical Investigations (July 2026) (Note: This guidance is largely geared to how to conduct trials in a way that can support psychedelic drug approval by FDA; it may be less relevant to other contexts.)
- HOPE Consensus Statement (Hopkins-Oxford Psychedelics Ethics Working Group)
- McGuire AL, et al., Developing an Ethics and Policy Framework for Psychedelic Clinical Care, JAMA Network Open, 2024
- Palitsky R, et al., A Framework for Assessment of Adverse Events Occurring in Psychedelic-Assisted Therapies, J Psychopharm, 2024
- Cheung K, et al. Informed Consent Documents from Psychedelic Trials: A Descriptive and Ethical Analysis, AJOB Emp Bioethics, 2025
- Psychedelic Alpha: www.psychedelicalpha.com

FOR MORE INFORMATION

These recommendations for IRB oversight of psychedelic administration research are based on empirical findings reported here:

- Robinson, J. O., Xiong, R. (Aria), Neitzke-Spruill, L., Purcell, A., Sisti, D., McGuire, A. L., & Fernandez Lynch, H. (2026). US Institutional Review Board Perspectives Regarding Psychedelic Research. *Psychedelic Medicine*. https://doi.org/10.1177/28314425261445746
- Neitzke-Spruill, L., Robinson, J.O., Purcell, A., Sisti, D., McGuire, A. L., & Fernandez Lynch, H. Investigators' Experiences with IRB Oversight of Psychedelic Research. Accepted at *Ethics and Human Research*. Preprint available on SSRN: https://dx.doi.org/10.2139/ssrn.7088898

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